Pinacolization and reduction of aromatic carbonyls with aluminium–KOH

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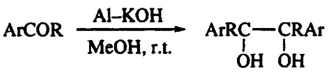
A simple and rapid procedure for the pinacolization of aromatic aldehydes and reduction of hindered ketones with inexpensive aluminium and KOH in methanol at ambient temperature is reported. The pinacolization and reduction are proposed to be proceeding *via* single electron transfer from aluminium.

Reduction of the carbonyl group has been known for a long time. A variety of reagents have been reported to reduce the carbonyl group to alcohols, glycols, methylene groups and also for the reductive coupling to alkenes. Pinacolization of carbonyls has been achieved by a number of reagents such as $Mg–MgI_2$,[1] $Zn–ZnCl_2$,[2] a number of transition metals, lanthanides and actinides.[3] Ti^{II} and Ti^{III} reagents have received considerable attention although olefination is a competing reaction with these reagents.[4] Reduction of carbonyls to alcohols can be achieved by catalytic hydrogenation, hydride transfer reagents, Meerwein–Pondorff–Verley reduction[5] and photochemical reductions.[6] The overall course of the reaction of carbonyls with metal reductants is determined by the fate of the initial ketyl radical anion.

Reductions of carbonyls with aluminium have also been reported and include reduction of cycloalkanones (4–6 membered) to the respective alcohols with aluminium amalgam in aqueous THF (the reductions are sensitive to the steric environment of the ketone),[7] ultrasound promoted aluminium amalgam reduction of phthalimides to hydroxy lactams[8] and classical pinacolizations, which use aluminium amalgam, by and large give unsatisfactory results.[9] Even benzophenone, benzaldehyde and acetophenone yield complex mixtures.[10] Recently, we communicated our initial results on the rapid pinacolization of carbonyls with aluminium–KOH.[10]

Results and discussion

In this paper, we report a rapid and inexpensive procedure for the pinacolization of aromatic aldehydes and acetophenones with aluminium powder and potassium hydroxide in methanol at ambient temperature. Diaryl ketones and methyl 1-napthyl ketone, however, underwent reduction under these conditions to the corresponding alcohols. No pinacolization or reduction was observed in the absence of KOH. Our results are listed in Tables 1 and 2. The reactions can be generalized as shown in eqns. (1) and (2).



$$ArCOR \xrightarrow[\text{MeOH, r.t.}]{\text{Al–KOH}} ArRC(OH)\text{—}C(OH)RAr \qquad (1)$$

Ar = Aryl; R = H, Me

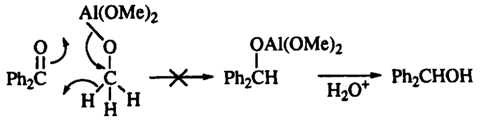
$$ArCOR' \xrightarrow[\text{MeOH, r.t.}]{\text{Al–KOH}} ArR'CHOH \qquad (2)$$

Ar = Aryl; Naphthyl; R = Aryl, Me

Methanol has been found to be the solvent of choice. No reduction or pinacolization was observed in THF or dioxane. But when methanol was replaced with ethanol, the reactions were found to be sluggish and yielded a mixture of the corresponding alcohols and 1,2-diols. The pinacolization of aromatic aldehydes and acetophenones is very rapid and gave nearly quantitative yields of 1,2-diols (Table 1). Most of the reactions rapidly went to completion (5–30 min) using 1:2:6 mol ratio of substrate to aluminium to KOH, although some required higher amounts of the reagent. No alcohol or carboxylic acid was observed to have been formed in these reactions due to competing Cannizaro's reaction because of the presence of KOH. There was also no olefin formation, except in the case of 9-anthraldehyde (run 11) presumably due to extended conjugation. The 1,2-diols are invariably a mixture of *meso*- and *dl*-stereoisomers. No significant change in the ratio of *meso*: *dl* was observed when the reactions were carried out in the presence of β-cyclodextrin.[11]

Table 2 lists the reactions of diaryl ketones which underwent reduction to the corresponding alcohols with aluminium–KOH unlike the reactions of aryl aldehydes which underwent rapid pinacolization. Even methyl 2-naphthyl ketone underwent reduction to give the corresponding alcohol (run 18). Anthrone, however, led to the formation of anthracene (run 22). The initially formed 9-anthrol undergoes rapid elimination of water under basic conditions to give anthracene. The distinct colour change from yellow to deep red to brown in this reaction is in agreement with our proposal. A complex mixture of products was obtained in the reactions of cyclohexanone (run 23) and octan-2-one (run 24) due to competing aldol type condensation.

We believed initially that pinacolization and reduction are proceeding by different pathways. Whereas pinacolization obviously appears to involve electron transfer from aluminium to the carbonyl group followed by rapid dimerization, the reduction could be proceeding *via* a 6-membered cyclic transition state (with aluminium trimethoxide formed *in situ*) similar to the Meerwein–Pondorff–Verley reduction. The possibility of such a pathway for reduction of carbonyls to give alcohols was, however, eliminated by a reaction of benzophenone with preformed aluminium trimethoxide, when the starting benzophenone was recovered unchanged even after prolonged reaction time [eqn. (3)].



(3)

It can also be conceived that the alcohols are obtained from more hindered ketones by a subsequent bond cleavage of the

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Table 1 Coupling of aromatic aldehydes and acetophenones to pinacols with aluminium–KOH

Run	ArCOR Ar	 R	Molar Ratio[a] ArCOR : Al	Reaction time[b]/ min	Yield (%)[c]	*dl*:*meso*[d]
1	Ph	H	1:2	5	87[12]	50:50
2	4-ClC_6H_4	H	1:2	5	93[13]	48:52
3	2-ClC_6H_4	H	1:2	15	82[14]	52:48
4	2-$MeOC_6H_4$	H	1:2	5	80[15]	52:48
5	4-$MeOC_6H_4$	H	1:2	5	98[16]	52:48
6	3,4-$(MeO)_2C_6H_3$	H	1:2	5	90[17]	50:50
7	4-MeC_6H_4	H	1:3	10	91[18]	50:50
8	3,4-(-OCH_2O-)C_6H_4	H	1:2	5	87[19]	—[e]
9	1-Naphthyl	H	1:3	15	78[20]	48:52
10	2-Naphthyl	H	1:3	15	83[21]	50:50
11	4-$Me_2NC_6H_4$	H	1:5	5	87[22]	—[e]
12	PhCH=CH	H	1:2	10	—[f]	
13	9-Anthryl	H	1:20	90	52[g,23]	—[e]
14	Ph	Me	1:3	10	89[12]	—[e]
15	4-MeC_6H_4	Me	1:5	10	87[24]	—[e]
16	4-$MeOC_6H_4$	Me	1:5	45	82[25]	50:50

[a] All the reactions were carried out in presence of potassium hydroxide (three mol equiv. of aluminium). [b] Monitored by complete disappearance of starting material using TLC. [c] Isolated yields; spectral data (IR, ^{1}H NMR) are in agreement with the structure. [d] Ratio of *dl*:*meso* as calculated from the ^{1}H NMR spectra. [e] ^{1}H NMR shows it to be pure *meso*-stereoisomer.[18] [f] Reaction was complete in 10 min but a tarry product was obtained. [g] A mixture of 1,2-diol (52%) and olefin (20%) was obtained on separation by silica gel column using benzene–light petroleum (70:30, v/v) as eluent.

Table 2 Reduction of aromatic ketones to alcohols with aluminium–KOH

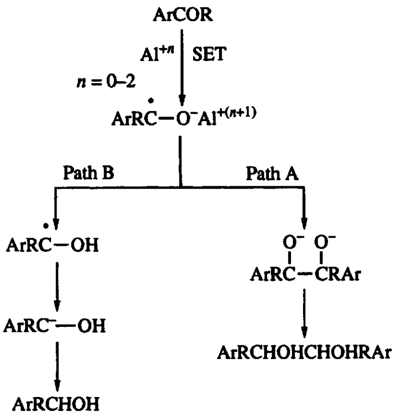
Run	Ketone	Mol ratio[a] (ArCOR : Al)	Reaction time[b]/min	% yield[c] (Alcohol)	Mp/°C Obs.	 Lit.
17	Benzophenone	1:3	30	88	64–66	66[12]
18	4-Chlorobenzophenone	1:3	30	89	61–62	62[26]
19	4,4′-Dichlorobenzophenone	1:5	30	90	92–93	94[12]
20	2-Amino-5-chlorobenzophenone	1:5	120	97	105	111–112[27]
21	Methyl 2-naphthyl ketone	1:3	90	77	74–75	73–78[12]
22	Fluorenone	1:3	15	90	153	153–154[12]
23	2,7-Dichlorofluorenone	1:3	15	93	158–159	161–162[28]
24	Xanthone	1:5	30	92	123–123	123[12]
25	Anthrone	1:10	30	65[h]	214	216[12]
26	Cyclohexanone	1:5	24[i]	—[j]	—	—
27	Octan-2-one	1:5	24[i]	—[j]	—	—

[h] The isolated product was identified to be anthracene. A distinct colour change from yellow to deep red to brown was observed in the reaction. [i] The reactions were carried out for 84 h. [j] The reaction mixture showed a number of spots on TLC and was discarded.

initially formed 1,2-diols as with other aldehydes. Therefore, a reaction of benzopinacol was carried out with aluminium–KOH in methanol under similar reaction conditions. The reaction mixture showed only the starting benzopinacol after 30 min whereas benzophenone undergoes complete reduction to benzhydrol in 30 min. Therefore, pinacolization followed by carbon–carbon cleavage for the reduction of carbonyls is also ruled out [eqn. (4)].

$$\mathrm{ArCOR} \not\longrightarrow \mathrm{ArRCHOHCHOHRAr} \longrightarrow \mathrm{ArRCHOH} \qquad (4)$$

Thus, we conclude that the pinacolization and reduction are proceeding by a similar pathway involving electron transfer from aluminium as shown in Scheme 1. The absence of pinacolization/reduction with aluminium in the absence of hydroxide ion suggests that either it could reduce the HOMO–LUMO difference of carbonyls or that it reacts with aluminium to give more reactive Al^+ and Al^{2+} which eventually transfers electrons to carbonyls. Path A involves the rapid dimerization of ketyl radical anion in the case of aldehydes and less hindered ketones while B involves a second electron transfer in case of diaryl ketones which give more highly resonance-stabilized carbanions, thus leading to the formation of alcohols. Higher reaction times in the case of hindered ketones is in agreement with our proposal. Bubbling oxygen through the reaction mixture of benzophenone with aluminium–KOH slowed the reaction and a reaction of 4-chlorobenzaldehyde with aluminium–KOH in methanol in the presence of cumene resulted in the formation of a mixture of 4-chlorobenzyl alcohol and 4,4′-dichlorohydrobenzoin. Both of these experiments also support our proposal of an electron transfer from aluminium.



Scheme 1

Experimental

All melting points were recorded on Tropical Labequip apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Perkin-Elmer model R-30 (90 MHz) and Hitachi FT-NMR

(60 MHz) spectrometers using Me_4Si as the internal standard. All the aldehydes and ketones were obtained from commercial sources and were used after distillation/recrystallization. Aluminium powder (SRL, 325 mesh), KOH (Qualigens) and methanol (Ranbaxy) were used in all the reactions.

General procedure for pinacolization/reduction of carbonyl compounds

In a 100 ml RB flask fitted with a water condenser and mounted over a magnetic stirrer were placed the carbonyl compound (10 mmol), aluminium powder and KOH (see Tables 1 and 2 for mol ratios). Methanol (10 ml per g of aluminium) was added to the contents of the flask and the reaction mixture was stirred. A vigorous reaction ensued immediately. The progress of the reaction was monitored for complete disappearance of the carbonyl compound by TLC. The reaction mixture was filtered to remove unreacted aluminium powder and water (*ca.* 100 ml) was added to the filtrate. A solid precipitated out which was filtered off at reduced pressure. The filtrate was extracted with dichloromethane (3 × 10 ml) and the combined dichloromethane extracts were dried over anhydrous $MgSO_4$. More product was obtained after removing the solvent on a Buchi rotary evaporator and drying the product in a vacuum desiccator. The product was identified by its mp and IR and NMR spectra.

In the reaction of 9-anthrone, the reaction mixture was filtered and the residue was washed with methanol (2 × 5 ml). The combined filtrate was dried (anhydrous $MgSO_4$), and concentrated on a rotary evaporator. The product mixture was charged on a silica gel column (100–200 mesh). The products were separated using light petroleum–benzene (1 : 1, v/v) as eluent. Anthracene (0.58 g, 65%) was obtained as confirmed by its mp 214 °C (lit. mp 216 °C) and mixed mp.

Reaction of benzophenone with aluminium trimethoxide

Aluminium trimethoxide was prepared by refluxing a mixture of aluminium foil (2.7 g, 100 mmol), $HgCl_2$ (0.05 g, 0.19 mmol) and dry MeOH (50 ml) until all the aluminium dissolved to give a grey suspension. CCl_4 (1 ml) was added to the boiling mixture which acts as a catalyst. The mixture was cooled to room temperature. Dry methanol was added to make the solution to 100 ml mark to obtain a 1 M solution of aluminium trimethoxide in methanol. The supernatant solution was used for the reaction. 20 ml of this solution (0.2 mol) was added to benzophenone (5 mmol, 0.91 g). The reaction mixture was stirred at ambient temperature and the progress of the reaction was monitored by TLC. No reaction was observed to have taken place by TLC using benzene as eluent even after 24 h and benzophenone was recovered unchanged.

Reaction of benzopinacol with aluminium–KOH

KOH (22.5 mmol, 1.262 g) was added to a mixture of benzopinacol (2.5 mmol, 0.915 g), aluminium powder (7.5 mmol, 0.202 g) and methanol (4 ml) and the reaction mixture stirred at ambient temperature. An exothermic reaction took place. The progress of the reaction was monitored by TLC using benzene as eluent which showed only one spot corresponding to benzhydrol after 3 h. The reaction was worked up as described in the general procedure. Benzhydrol (0.78 g, 83%) was obtained as confirmed by its mp 65 °C, (lit. mp 66 °C) and NMR spectra.

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